Systematic optimization of human pluripotent stem cells media using Design of Experiments.

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Public Summary:
Here we described a novel method to optimize culture conditions for human pluripotent stem cells, using a mathematical and statistical method. The systematic optimization revealed a new formulation, called iDEAL, able to maintain human pluripotent stem cells in better condition than previous media. The new media is also more affordable, xenon-free, easy to make, allowing a broader use of human stem cells around the world.

Scientific Abstract:
Human pluripotent stem cells (hPSC) are used to study the early stages of human development in vitro and, increasingly due to somatic cell reprogramming, cellular and molecular mechanisms of disease. Cell culture medium is a critical factor for hPSC to maintain pluripotency and self-renewal. Numerous defined culture media have been empirically developed but never systematically optimized for culturing hPSC. We applied design of experiments (DOE), a powerful statistical tool, to improve the medium formulation for hPSC. Using pluripotency and cell growth as read-outs, we determined the optimal concentration of both basic fibroblast growth factor (bFGF) and neuregulin-1 beta 1 (NRG1beta1). The resulting formulation, named iDEAL, improved the maintenance and passage of hPSC in both normal and stressful conditions, and affected trimethylated histone 3 lysine 27 (H3K27me3) epigenetic status after genetic reprogramming. It also enhances efficient hPSC plating as single cells. Altogether, iDEAL potentially allows scalable and controllable hPSC culture routine in translational research. Our DOE strategy could also be applied to hPSC differentiation protocols, which often require numerous and complex cell culture media.